UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/686,020	10/10/2000	Jennifa Gosling	19934000710	4696

20350 7590 04/07/2004

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/686,020	GOSLING ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed* after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-43* is/are pending in the application.

4a) Of the above claim(s) *38-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-37 and 44-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *33-43* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/22/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 22 September 2003 has been entered in full. Claims 33 and 35 are amended.

This application contains claims 38-43 drawn to an invention nonelected without traverse in the paper of 27 January 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant continues to traverse the Restriction requirements set forth in the Paper of 26 December 2002. Upon allowance of the elected species, applicant will be entitled to consideration of claims to additional species until all species have been examined or a non-allowable species is found. If Applicant wishes to pursue the matter further, a petition should be filed in accordance with 37 CFR 1.144. The requirement is still deemed proper and is therefore made FINAL. (Please also see Claim Objections, below.)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 33-37 and 44-48 are under consideration in the instant application, as they read upon the species of ELC and inflammation.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 2-3 of the previous Office Action (21 April 2003) are *withdrawn* in view of the amended hyperlinks and brief description of drawings (22 September 2003).

2. The objections to the claims at pg 3 of the previous Office Action (21 April 2003) are *withdrawn in part* in view of the amended claims (22 September 2003). Please see Claim Objections, below.

3. The rejections to claims 33-37 and 44-48 under 35 U.S.C. § 112, second paragraph at pg 8 of the previous Office Action (21 April 2003) are *withdrawn* in view of the amended claims (22 September 2003).

Claim Objections

4. Claims 33-37 and 47-48 are objected to because of the following informalities:

4a. Claims 33-37 and 47-48 recite non-elected species. The basis for this objection is set forth at pg 3 of the previous Office Action (21 April 2003).

Applicant's arguments (22 September 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that examination may have been limited to ELC and inflammatory diseases (species). Applicant contends that the full breadth of the claims should have been examined. Applicant argues that MPEP 803.02 emphasizes that in Markush type claims, such as claims 33 and 35, that examination must continue with respect to all species unless prior art is identified that anticipates the claim or renders it obvious. Applicant submits that the Office did not identify any prior art and thus examination should have continued with respect to non-elected species until all species had been examined on the merits or until prior art with respect to one species was found.

Applicant's arguments have been fully considered but are not found to be persuasive. Non-elected species will not be searched because an art search for every species will not overlap. Each binding molecule and CCX CKR-mediated condition is unique, requiring a unique search

of the prior art. Searching all of the species in a single patent application would provide an undue search burden on the Examiner and the USPTO's resources because of the non-coextensive nature of these searches. Following Applicant's species election, the claims were examined to the extent that they read upon the elected species. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If Applicant wishes to pursue the matter further, a petition should be filed in accordance with 37 CFR 1.144.

Claim Rejections - 35 USC § 112, first paragraph

5. Claims 33-37 and 44-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The basis for this rejection is set forth at pg 3-6 of the previous Office Action (21 April 2003).

Specifically, the claims are directed to a method of treating an CCX CKR-mediated condition in a mammal comprising administering to the mammal an agent that inhibits or promotes the binding of CCX CKR to ELC (EBI-1-ligand chemokine) in a cell or tissue in the mammal whereby inhibition or promotion of binding ameliorates the CCX CKR-mediated condition. The claims also recite that the CCX CKR-mediated condition is inflammation. The claims recite that the mammal is a human or non-human primate and that the agent is an antibody.

Applicant's arguments (22 September 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant contends that the specification at pg 44, lines 1-13 provides guidance on appropriate dosage of an agent. Applicant also indicates that at pg 44, lines 11-13 of the specification, disclosure is provided with respect to duration and frequency of administration. Applicant states that the specification describes a variety of modes of administration (pg 41-43) and that several references provide guidance on formulations, dosages, and modes of administration (pg 41, lines 6-12).

Applicant's arguments have been fully considered but are not found to be persuasive. The specification discloses, for example, that "In the treatment or prevention of conditions which require chemokine receptor modulation an appropriate dosage level will generally be about 0.001 to 100 mg per kg patient body weight per day which can be administered in single or multiple doses. Preferably, the dosage level will be about 0.01 to about 25 mg/kg per day; more preferably about 0.05 to about 10 mg/kg per day. A suitable dosage level may be about 0.01 to 25 mg/kg per day, about 0.05 to 10 mg/kg per day, or about 0.1 to 5 mg/kg per day. Within this range the dosage may be about 0.005 to about 0.05, 0.05 to 0.5 or 0.5 to 5 mg/kg per day" (pg 44, lines 1-7). Such broad brush assertions do not constitute adequate guidance to practice the claimed method, but rather constitute an invitation to experiment empirally to determine how to practice the suggested method to obtain the therapeutic results required by the claims. The specification discloses numerous modes of administration (pg 41-43) as well as a broad range of dosage amounts. Although Applicant submits that parameters such as dosages and timing and methods of administration of therapeutic agents may need to be optimized and that optimization is routine, there is little guidance in the specification for one skilled in the art to determine these optimal conditions. Such trial and error experimentation is considered undue.

(ii) Applicant argues that pg 38 of the specification show chemical structures for both agonists and antagonists of ligand binding to CCX CKR. Applicant asserts that the specification provides specific chemical structures of compounds that modulate the binding of certain ligands to CCX CKR. Applicant also submits that the specification provides extensive guidance on how additional compounds can be identified using a variety of screening assays and model systems (pg 16; pg 33-38, example 7). Applicant states that the specification provides guidance on a variety of different types of molecules that can be utilized in the current methods, including antisense polynucleotides, ribozymes, and antibodies.

Applicant's arguments have been fully considered but are not found to be persuasive. Although the chemical structures of three compounds are disclosed at pg 38 of the specification, these compounds are not a representative number of species to support the description of an entire genus of agents (as recited in the claims) which incorporate, for example, nucleic acid molecules, proteins (such as growth factors), antibodies, and other organic and inorganic substances. Additionally, the claims, which recite that the agent inhibits or promotes the binding of CCX CKR to ELC, are not commensurate in scope with the invention disclosed in the instant specification. The specification teaches that " 'exemplary small molecule' modulators of CCX CKR binding to ELC were identified. These compounds, or structurally related compounds, are used as modulators (agonists or antagonists) of CCX CKR activity, in assays to identify other modulators and agents, to further characterize the CCX CKR, and for identification of structurally related modulators with greater or different activity" (pg 38, lines 1-6). There is little guidance in the specification to indicate that the compounds at pg 38 inhibit or promote the binding of CCX CKR to ELC. According to the specification, these compounds modulate CCX CKR activity rather than CCX CKR binding to ELC. Furthermore, the specification's general

discussion of screening for additional compounds (pg 16, pg 33-38) constitutes an invitation to experiment by trial and error. The skilled artisan must resort to trial and error experimentation to generate the infinite number of agents, as recited in the claims, and to screen them for a desired activity (e.g., inhibiting or promoting binding of CCX CKR to ELC). Such trial and error is considered undue.

(iii) Applicant contends that the specification provides an extensive discussion of diseases that can be mediated by CCX CKR activity. Applicant indicates that since CCX CKR is a chemokine receptor, this receptor would be expected to be involved in those diseases correlated with chemokine activity (pg 1, lines 18-23). Applicant also asserts that the specification identifies a number of specific diseases associated with activities such as inflammatory responses, leukocyte trafficking, and angiogenesis, that can be treated with CCX CKR modulators (pg 39, line 19 to pg 40, line 17). Applicant indicates the submission of several articles that discuss the role certain chemokines (identified in the current application as ligands for CCX CKR) can play in a variety of diseases. Weninger et al. (J Immunol 170: 4638-4648, 2003) discusses the role that CCL19 (ELC) and CCL21 (SLC) have in various diseases associated with T cell recruitment. Hjelmstrom et al. (Am J Pathol 156: 1133-1138, 2000) describes the involvement of ELC and BLC in various types of chronic inflammation. Xanthou et al. (Arthritis and Rheumatism 44: 408-418, 2001) describes the results implicating ELC in a particular inflammatory disease of the salivary glands.

Applicant's arguments have been fully considered but are not found to be persuasive. The Examiner acknowledges that chemokines, such as ELC (CCL19), may play a role in conditions such as Sjogren's syndrome or chronic inflammatory diseases (Katou et al., J Pathol

199:98-106, 2003; Weninger et al., Xanthou et al.). However, these results do not substantiate a role for CCX CKR in such diseases. The state of the art is also such that ELC and the various chemokines recited in the claims bind to receptors other than CCX CKR of the instant application. For example, Baggiolini (J Internal Med 250: 91-104, 2001) teaches that ELC binds CCR7 (Table 2). Therefore, one skilled in the art would not be able to determine if the putative CCX CKR of the instant application or CCR7 is involved in a disease. Furthermore, the specification discloses numerous possible conditions and diseases that could be treated with a modulator of CCX CKR (pg 39-40). However, the specification does not disclose any conditions or diseases that are *specifically* associated with altered levels or forms of the CCX CKR. The specification also does not identify a CCX CKR-mediated condition that has the binding of CCX CKR to ELC as a rate limiting step. Significant further experimentation would be required of the skilled artisan to identify a CCX CKR-mediated condition and individuals with such a disease. Therefore, the specification does not provide enabling guidance regarding how to select a subject.

(iv) Applicant asserts that the specification describes a number of specific conditions that can be correlated with CCX CKR activity. Applicant contends whether a specific agent is useful in treating a particular disease can be determined without undue experimentation by testing the agent with various *in vivo* model systems known in the art, including, for instance, those described in the specification for various diseases (pg 36, lines 16-24).

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed above, the specification discloses numerous possible conditions and diseases that could be treated with a modulator of CCX CKR (pg 39-40). However, the specification does not

disclose any conditions or diseases that are *specifically* associated with altered levels or forms of the CCX CKR. Although various *in vivo* model systems for diseases such as inflammation are known in the art, the specification has not established a nexus between CCX CKR and inflammation or any other disease. Therefore, significant further experimentation would be required of the skilled artisan to identify a CCX CKR-mediated condition and individuals with such a disease. Such experimentation is considered undue. Additionally, since the specification does not associate a specific condition or disease with CCX CKR, undue experimentation would be required of the skilled artisan to determine whether to inhibit the binding of the ligands (such as ELC) to the receptor or to promote the binding of the ligands to the receptor.

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to identify a CCX CKR-mediated condition that requires the binding of CCX CKR to ELC as a rate limiting step, to identify subjects with a CCX CKR-mediated condition, to identify and administer agents that would inhibit/promote binding of CCX CKR to ELC and treat the condition, and to determine the mechanism of action of the agent (i.e., inhibition or promotion), the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations on a specific CCX CKR-mediated condition and the mechanism of action of the agent necessary for treatment of that condition, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

6. Claims 33-37 and 44-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pg 6-8 of the previous Office Action (21 April 2003).

The claims are directed to a method of treating an CCX CKR-mediated condition in a mammal comprising administering to the mammal an agent that inhibits or promotes the binding of CCX CKR to ELC (EBI-1-ligand chemokine) in a cell or tissue in the mammal whereby inhibition or promotion of binding ameliorates the CCX CKR-mediated condition. The claims also recite that the CCX CKR-mediated condition is inflammation. The claims recite that the mammal is a human or non-human primate and that the agent is an antibody.

Applicant's arguments (22 September 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the specification provides several structures of molecules that inhibit or promote binding between CCX CKR and a ligand.

Applicant's arguments have been fully considered but are not found to be persuasive. Although the chemical structures of three compounds are disclosed at pg 38 of the specification, these compounds are not a representative number of species to support the description of an entire genus of agents (as recited in the claims) which incorporate, for example, nucleic acid molecules, proteins (such as growth factors), antibodies, and other organic and inorganic substances. As discussed above, there is little guidance in the specification to indicate that the compounds at pg 38 inhibit or promote the binding of CCX CKR to ELC. According to the specification, these compounds modulate CCX CKR activity rather than CCX CKR binding to ELC (pg 38, lines 1-6). Furthermore, the broad brush discussion of screening for additional compounds (pg 16, pg 33-38) does not constitute a disclosure of a representative number of

members. No such compounds were made or shown to have activity. The specification's general discussion of making and screening for compounds constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

(ii) Applicant contends that the structure of antisense molecules and triplex oli- and polynucleotides that can be utilized in certain methods are directed based upon the nucleic acid sequence of CCX CKR, which is provided in the specification. Applicant argues that the specification describes which segments of CCX CKR these agents are designed to bind to and how many nucleotides these types of agents typically include. Applicant submits that based upon this disclosure and the additional guidance provided in the cited references regarding molecular design and use of such molecules in treatment (pg 25, lines 6-9 and 21-25; pg 25, line 34 to pg 26, line 3), one of skill can envision appropriate molecules. One of ordinary skill can also envision suitable ribozymes that could be used to inhibit CCX CKR because the structure of such ribozymes also depends upon the sequence of CCX CKR, which is provided in the current application. Applicant also argues that from the protein structure information provided in the specification for CCX CKR and the known sequence of CCX CKR ligands, those of ordinary skill in the could envision suitable antibodies that would inhibit binding of CCX CKR with its cognate ligands.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification teaches "methods of treating CCX CKR-mediated conditions or diseases by administering to a subject having such a disease or condition, a therapeutically effective amount of a modulator of CCX CKR function, i.e., agonists (stimulators) and antagonists (inhibitors) of CCX CKR function or gene expression" (pg 2-5). The specification discloses that modulators of

CCX CKR function include small molecules agonists and antagonists of CCX CKR function, polypeptide inhibitors, antisense, ribozyme, and triplex polynucleotides, gene therapy, etc. (pg 39, lines 6-9). However, the brief description in the specification of a few examples of agents that could be administered to a subject is not adequate written description of an entire genus of agents, both organic and inorganic. Additionally, the specification of the instant application only discloses general guidance as to the design of antisense molecules and triplex olig- and polynucleotides that could be used in the methods (pg 23-25). Again, the specification only discloses general guidance as to the structure and design of ribozymes and antibodies (pg 26, pg 29-32). The skilled artisan cannot envision the infinite number of agents encompassed by the claimed methods, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The agent itself is required.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BEB
Art Unit 1647
04 March 2004

Gary L. Kunz

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/686,020	10/10/2000	Jennifa Gosling	19934000710	4696

20350 7590 04/21/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

double check → didn't we have an interview in this case?

no 09/721,341

- find refs stating ELC binds other receptors besides CCK CLR

Non-Final

Office Action Summary	Application No.	Applicant(s)	
	09/686,020	GOSLING ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-48* is/are pending in the application.

4a) Of the above claim(s) *38-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-37 and 44-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *33-48* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12,13*.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Election/Restrictions

Applicant's election of the species ELC and inflammation in Paper No. 19 (27 January 2003) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 38-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 19 (27 January 2003).

It is noted to Applicant that upon allowance of the elected species, applicant will be entitled to consideration of claims to additional species until all species have been examined or a non-allowable species is found.

Claims 33-37 and 44-48 are under consideration in the instant application, as they read upon the species of ELC and inflammation.

Drawings

1. The formal drawings were received on 27 January 2003 (Paper No. 18). These drawings are acceptable.

Specification withdraw

2. The disclosure is objected to because of the following informalities:

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. (See pg 13, line 31; pg 51, lines 23-24; pg 53, line 22)

Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

4. The Brief Description of Drawings for Figure 4 at pg 5-6 of the specification does not refer to Figure 4A.

Appropriate correction is required.

Claim Objections

5. Claims 33-37 and 47-48 are objected to because of the following informalities:

5a. Claims 33-37 and 47-48 recite non-elected species.

5b. Claim 33, line 1 recites "treating an CCX CKR-mediated condition". However, to be more grammatically correct, the claim should be amended to recite "treating a CCX CKR-mediated condition".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 33-37 and 44-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Specifically, the claims are directed to a method of treating an CCX CKR-mediated condition in a mammal comprising administering to the mammal an agent that inhibits or

promotes the binding of CCX CKR to ELC (EBI-1-ligand chemokine) in a cell or tissue in the mammal. The claims also recite that the CCX CKR-mediated condition is inflammation. The claims recite that the mammal is a human or non-human primate and that the agent is an antibody.

The specification of the instant application teaches "methods of treating CCX CKR-mediated conditions or diseases by administering to a subject having such a disease or condition, a therapeutically effective amount of a modulator of CCX CKR function, i.e., agonists (stimulators) and antagonists (inhibitors) of CCX CKR function or gene expression. Such modulators include small molecules agonists and antagonists of CCX XKR function; polypeptide inhibitors; antisense, ribozyme, and triplex polynucleotides; gene therapy, and the like" (pg 39, lines 1-9). The specification also teaches the modulators CCX CKR activity can inhibit the proliferation and differentiation of cells involved in an inflammatory response (pg 39, lines 30-31). However, this prophetic procedure is not adequate guidance, but is merely an invitation for the artisan to use the current invention as a starting point for further experimentation. For example, the prophetic example does not teach the skilled artisan the optimal dosage, duration, and mode of administration of any agent to any mammal. Furthermore, the claimed method may not necessarily treat a CCX CKR-mediated condition, such as inflammation. The skilled artisan must resort to trial and error experimentation to determine the optimal dosage, duration, and mode of administration of all possible agents that inhibit or promote binding of CCX CKR to ELC. Such trial and error experimentation is considered undue. According to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed."

not a rep. number of species

Additionally, the specification does not disclose any conditions that are specifically associated with altered levels or forms of the CCX CKR. The specification also does not identify a CCX CKR-mediated condition that has the binding of CCX CKR to ELC as a rate limiting step. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Furthermore, there are no agents disclosed that interrupt or otherwise modulate binding of CCX CKR to ELC. Therefore, the specification does not provide enabling guidance regarding how to select an agent or patient.

The specification teaches that CCX CKR is internalized in the presence of ELC, SLC, TECK, and CTACK (pg 59, Example 8). However, there are also no methods or working examples in the specification indicating the mechanism of action required by the agent for treatment of a CCX CKR-mediated condition. For example, in order to treat a CCX CKR-mediated condition, does the agent inhibit the binding of the ligands to the receptor and therefore, inhibit internalization? Or, does the agent promote the binding of the ligands to the receptor and therefore, promote internalization of the receptor? Since the specification does not associate a specific condition with CCX CKR, undue experimentation would be required of the skilled artisan to identify such a disease and determine whether to inhibit the binding of the ligands (such as ELC) to the receptor or to promote the binding of the ligands to the receptor.

Due to the large quantity of experimentation necessary to identify a CCX CKR-mediated condition that requires the binding of CCX CKR to ELC as a rate limiting step, to identify individuals with a CCX CKR-mediated condition, to identify and administer agents that would inhibit/promote binding of CCX CKR to ELC and treat the condition, and to determine the mechanism of action of the agent (i.e., inhibition or promotion), the lack of direction/guidance

presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations on a specific CCX CKR-mediated condition and the mechanism of action of the agent necessary for treatment of that condition, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

7. Claims 33-37, 44-45, and 47-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the claims are directed to a method of treating an CCX CKR-mediated condition in a mammal comprising administering to the mammal an agent that inhibits or promotes the binding of CCX CKR to ELC (EBI-1-ligand chemokine) in a cell or tissue in the mammal. The claims also recite that the CCX CKR-mediated condition is inflammation. The claims recite that the mammal is a human or non-human primate and that the agent is an antibody.

As discussed above, the specification only teaches "methods of treating CCX CKR-mediated conditions or diseases by administering to a subject having such a disease or condition, a therapeutically effective amount of a modulator of CCX CKR function, i.e., agonists (stimulators) and antagonists (inhibitors) of CCX CKR function or gene expression. Such modulators include small molecules agonists and antagonists of CCX XKR function; polypeptide inhibitors; antisense, ribozyme, and triplex polynucleotides; gene therapy, and the like" (pg 39,

lines 1-9). However, the specification does not teach any specific agents that are capable of inhibiting or promoting the binding of CCX CKR to ELC to treat a CCX CKR-mediated condition. The brief description in the specification of a few examples of agents that could be administered to an individual is not adequate written description of an entire genus of agents, both organic and inorganic.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the infinite number of agents encompassed by the claimed methods, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The agents itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

Therefore, only a specific agent, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath*

makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). withdrawn

35 USC § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 33-37 and 44-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Regarding claims 33-37 and 44-48, the acronym "CCX CKR" renders the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

11. Claims 33-37 and 44-48 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating that administration of an agent treats a CCX CKR-mediated condition.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
April 11, 2003

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER